UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/646,362	08/21/2003	Xian-Ming Zeng	TEVNHC 3.0-585	8631

530 7590 08/06/2008

LERNER, DAVID, LITTENBERG,
KRUMHOLZ & MENTLIK
600 SOUTH AVENUE WEST
WESTFIELD, NJ 07090

EXAMINER	
ALSTRUM ACEVEDO, JAMES HENRY	
ART UNIT	PAPER NUMBER
1616	
MAIL DATE	DELIVERY MODE
08/06/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/646,362	ZENG, XIAN-MING	
	Examiner	Art Unit	
	JAMES H. ALSTRUM ACEVEDO	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 8-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/29/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-6 and 8-16 are pending. Applicant previously cancelled claim 7. Applicant amended claims 6, 11, and 14-15. Claim 16 is new. Receipt and consideration of Applicants new IDS (submitted 4/29/08), amended claim set, and remarks/arguments, submitted on July 7, 2008 are acknowledged. All rejections not explicitly maintained in the instant office action have been withdrawn per Applicants' claim amendments.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 1-2, 5-6, and 8-10 under 35 U.S.C. 102(b) as being anticipated by Haeberlin (WO 01/39745) **is maintained** for the reasons of record, which are restated and further articulated below.

Applicants claim (1) a dry powder composition comprising (a) at least about 0.25% w/w of an active ingredient with a particle size of less than 10 microns in diameter and (b) a pharmaceutically acceptable particulate carrier with a particle size of less than 250 microns in diameter (claim 1) or wherein the active is present in an amount less than 10% w/w (claim 2), wherein the active is formoterol or a pharmaceutically acceptable salt thereof (claim 6), the carrier is lactose (claim 5); (2) a capsule containing from 1-25 mg of a dry powder composition

of claim 1 or 4 (claim 8); (3) a MDPI (i.e. a multidose dry powder inhaler) comprising a reservoir containing the dry powder of claim 1 or 4 (claim 9); and (4) a method for the treatment of chronic obstructive pulmonary (COPD) disease by the step of administering the dry powder of claim 1 or 4 (claim 10).

Haeberlin discloses dry powder formulations that are particularly effective for the **treatment of COPD** when administered by inhalation as **a dry powder comprising formoterol in admixture with a diluent or carrier in an amount of 400 micrograms to 5,000 micrograms per microgram of formoterol active** (pg 1, 2nd paragraph). A composition comprising 400 micrograms of diluent and 1 microgram of formoterol active comprises **0.25% w/w active**. Formoterol may be in the form of its free base or in the form of a **pharmaceutically acceptable salt** (pg. 2, lines 1-3). A particularly preferred formoterol salt is **formoterol fumarate**, especially formoterol fumarate dihydrate (pg. 2, 2nd paragraph beginning on said page). **Suitable diluents or carriers include lactose** (pg. 2, last three lines of said page). Lactose is a preferred diluent (pg. 3, line 1). The mean particle diameter of formoterol active (A) is preferably up to 10 microns, especially preferably 1-5 microns (pg. 3, lines 4-6). The **diluent or carrier (B)** has a maximum diameter of 300 microns, **preferably a maximum diameter of 212 microns** (pg. 3, lines 6-8). In a preferred embodiment the dry powder is in a capsule containing a unit dose of (A), wherein the amount of diluent/carrier is preferably such that the **total weight of the dry powder per capsule is between 5 mg to 25 mg** (pg. 3, 2nd paragraph). Doses of formoterol active may be from 1 microgram to 60 micrograms (pg. 3, 2nd paragraph). In another preferred embodiment **the dry powder is in a reservoir of a multi-dose dry powder inhaler (i.e. MDPI)** adapted to deliver a unit dose (pg. 4, 2nd paragraph). Multi-dose dry powder

inhalers are well known in the art and commercially available (pg. 4, 2nd paragraph). Gelatin capsules containing dry powder compositions comprising formoterol fumarate dihydrate in admixture with lactose monohydrate are exemplified in Examples 1-29. Example 6 discloses a composition wherein the formoterol active is present in an amount of 0.24% w/w.

Response to Arguments

Applicant's arguments filed April 15, 2008 have been fully considered but they are not persuasive. Applicants have traversed the instant rejection by asserting that the amount of active agent disclosed by Haeberlin allegedly does not touch the range claimed by Applicants (i.e. allegedly the amount disclosed by Haeberlin is 0.249% vs. Applicants' required minimum of 0.25%). In support of Applicant's arguments, Applicant has cited Atofina v. Great Lakes Chem. Corp., 441, F. 3d 991 (Fed. Cir. 2006) ("Atofina").

The Examiner respectfully disagrees with Applicants' traversal argument; because when fairly comparing calculated numerical values it is imperative that one utilize the same number of significant figures. Applicants' claimed minimum is only recited to two significant figures, thus it is inappropriate to calculate a figure for the prior art and report it using three significant figures. When Applicants' calculation is repeated and limited to two significant figures, the prior art value touches Applicants' claimed range. Applicant's citation of Atofina is noted, but it is believed that the facts of Atofina are not dispositive to the instant fact pattern, because Atofina discussed a broad prior art range encompassing a much smaller claimed range, wherein the prior art range did not touch any point of the claimed range. The situation here is different, because the prior art disclosure is sufficiently specific to a single point within Applicant's claimed range

(i.e. a minimum amount of active of 0.25%. Thus, the instant rejection is deemed to remain proper.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejection of claims 1-6 and 8-15 under 35 U.S.C. 103(a) as being unpatentable over Haeberlin (WO 01/39745) **is maintained** for the reasons articulated below. Claim 16 is appended to this rejection. Thus, **claims 1-6 and 8-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haeberlin (WO 01/39745)** for the reasons of record restated and further articulated below.

Applicant Claims

Applicant's claims 1-2 and 5-10 have been described above in the rejection under 35 U.S.C. §102(b) as being anticipated by Haeberlin. In claims 3-4, Applicant claims dry powder compositions wherein the composition comprises about 0.26 % to about 1% w/w active (claim 3) or about 0.265 % to about 0.5 % w/w active (claim 4), wherein "about" is defined in [0019] of the instant specification to mean a variance of 5% of both the upper and lower limits of stated values in a range of values.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The disclosures of Haeberlin have been restated above in the instant application.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Haeberlin lacks the teaching of dry powder compositions comprising about 0.26% w/w to about 1% w/w active ingredient.

Finding of Prima Facie Obviousness Rational and Motivation

(MPEP §2142-2143)

It would have been obvious to a person of ordinary skill in the art at the time of the instant invention to optimize the amounts of formoterol in the compositions of Haeberlin according to the needs of subjects in need of administration of formoterol, for example, subjects in need of administration of formoterol to treat COPD. The ratio of formoterol to diluent/carrier disclosed on page 1 of Haeberlin is described as a particularly effective formulation for the treatment of COPD, however, this description of the dry powder compositions as being "particularly effective" does not constitute a teaching away from compositions having greater amounts of formoterol active relative to the diluent/carrier. The amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient needed to achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, the optimization of ingredient amounts would have been obvious at the time of applicant's invention.

Response to Arguments

Applicant's arguments filed April 15, 2008 have been fully considered but they are not persuasive. Applicants have traversed the instant rejection by asserting that it is not reasonable to optimize the maximum amount of formoterol disclosed by Haeberlin to higher values and implicitly arguing that the teachings of Haeberlin reciting a "particularly effective" amount of active agent allegedly would preclude or discourage the ordinary skilled artisan from using a

greater amount of active agent. Applicant has also argued that Applicant has demonstrated that Applicant's invented compositions [surprisingly] exhibit more accurate metering, and greater uniformity and consistency in the powder dispersions when dispensed from MDPI devices.

The Examiner respectfully disagrees with Applicants' traversal argument. Regarding the previously stated optimization of the amount of formoterol, this statement is retracted. It would have been well within the capability of the ordinary skilled artisan to adjust the amount of active agent in a dry powder formulation per the needs of subjects in need of treatment and said subjects' response to treatment. Furthermore, the modification of the amount of active in a composition is an obvious way to increase the amount of active agent administered to a subject as well as modifying the amount of a given active agent administered. Applicants have not demonstrated any particular criticality regarding the amount of active agent present in the claimed composition. Applicants have not asserted that amounts of active greater than 0.25% w/w yield unexpected or surprising results or that compositions comprising amounts of active below 0.25% w/w exhibit undesirable properties. Applicants' general statements in paragraph [0008] are not persuasive as to the alleged superior properties of the claimed composition, but merely represent unsubstantiated allegations of superiority. Regarding the FPF fractions recited in claims 14-15, Haeberlin is silent. Applicants are reminded that the Office lacks laboratory facilities to test the compositions invented by Haeberlin to determine the FPF that these would exhibit upon administration from an IVAX® MDPI, as was used by Applicants in their determination of the FPF of their invented formoterol fumarate dihydrate compositions. It is noted that Applicant has not provided any probative ***comparative*** evidence as to the implied surprising properties of greater accurate dosing and dosing uniformity and consistency upon

actuation from a MDPI device. Without a proper side-by-side comparison data with the closest prior art, it cannot be determined whether Applicant's data is properly considered to show any surprising or unexpected results. Thus, the instant rejection is deemed to remain proper and is maintained.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The provisional rejection of claims 1, 4-6, and 9 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 9-11 of copending Application No. 10/646,361 (copending '361) in view of Haeberlin (WO 01/39745) **is maintained** for the reasons of record and because Applicants did not traverse the instant rejection with any substantive arguments.

Conclusion

Claims 1-6 and 8-16 are rejected. No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

J.H.A.-A.
Patent Examiner
Technology Center 1600

/Johann R. Richter/
Supervisory Patent Examiner, Art Unit 1616